request that the Examiner forward the PTO form 948, or indicate the drawings are acceptable and need no revisions in the next Office Action.

II. Restriction Requirement

In the Office Action mailed August 29, 2001, the Examiner required restriction to one of Groups I - IV under 35 U.S.C. § 121. Applicants respectfully traversed the restriction requirement, and provisionally elected the claims of Group III (claims 79-81, 91, 94, 96, 97, 100, 102, 103, 106, 108, 109, 112, 114, 115, 118, 120, 121, 124 and 126), which encompasses SEQ ID NO.: 3, for further prosecution. The Patent Office maintained the restriction requirement in the Office Action dated March 4, 2002, asserting the inventions encompassed by each of these sequence listings were "not disclosed as capable of being used together and also, the inventions have different modes of operation, different function and different effects" and that a search of each "would require a separate nucleotide search." Applicants note the Examiner now asserts that SEQ ID NOs.: 1, 2, and 34 are "portions of the 5' regulatory region of the TIGR gene" in Office Action dated September 10, 2002 at page 4, lines 2-3. This assertion is inconsistent with the position taken by the Patent Office in the restriction requirement. Applicants respectfully submit that if SEQ ID NOs.: 1, 2, and 34 are "portions of the 5' regulatory region of the TIGR gene" as the Examiner contends, then a single search of the TIGR regulatory region would suffice to examine all of these sequences.

Applicants again respectfully submit that the complete examination of the application would be most expeditiously handled by treating all of the pending claims as a single entity, and that there is no undue burden in search the entire application. As Section 803 of the MPEP states, "[i]f the search and examination of an entire application can be made without serious burden, the

Examiner must examine it on the merits. . . ." In view of the foregoing, Applicants respectfully request reconsideration of the restriction requirement.

III. Claim Objections

Applicants note the Examiner's indication that dependent claims 94, 115, 118, and 120 would be allowable if rewritten in independent form and the objection to these claims as depending from a rejected base claim. Applicants further note the objection to claims 115 and 118 as being substantial duplicates. In order to be fully responsive to the Office Action, Applicants respectfully request that these objections be held in abeyance until the Examiner has considered the Applicants' arguments.

IV. Rejection of Claims 1-2 and 10-22 under 35 U.S.C. §112, 1st Paragraph: Written Description

Claims 79-81, 91, 96, 97, 100, 102, 103, 106, 108, 109, 112, 114, 115, 118, 121, 124, and 126 stand rejected under 35 U.S.C. §112, first paragraph, as allegedly containing subject matter that was not described in the specification in a manner that reasonably conveys to one of ordinary skill in the art that the inventors had possession of the claimed invention at the time of filing.

In the Office Action Dated September 10, 2002, the Examiner alleges that the claims lack written description support under §112 first paragraph as they "are drawn to fragments and sequences comprising fragments of or the sequences of comprising SEQ ID NO.: 3 or fragments thereof, vectors and cells expressing said constructs, which are not considered adequately described by the specification as filed." The Examiner further alleges the specification does not teach "specific regions by way of sequence structure which correlate to functional regions for initiation of TIGR gene expression," and "sequences comprising SEQ ID NO.: 3 for instance containing the gene coding region for the TIGR gene." Relying on MPEP 2163 the Examiner

additionally alleges the claims fail to meet the written description requirement as the "invention as a whole, any nucleic acid fragment of SEQ ID NO.: 3 or any larger sequence comprising SEQ ID NO.: 3, is not adequately described in view of the lack of disclosure of specific identifying characteristics" and the inability of an artisan to "immediately envisage the sequence of any mutation, addition or deletion from SEQ ID NO.: 3 having the same functional properties."

Compliance with written description is essentially a fact-based inquiry. *See Enzo Biochem, Inc., v. Gen-Probe Inc.*, 296 F.3d 1316, 1324 (Fed. Cir. 2002) (citing *Vas-Cath Inc. v. Mahurkar*, 935 F.2d 1555, 1563 (Fed. Cir. 1991) and *In re DiLeon*, 436 F.2d 1404,1405 (C.C.PA. 1971)). Disclosure of "such descriptive means as words, structures, figures, diagrams formulas, etc., that fully set forth the claimed invention" satisfies the written description requirement. *See, Enzo Biochem*, 296 F.3d at 1329 (quoting from *Lockwood v. American Airlines, Inc.*, 107 F.3d 1565, 1571 (Fed. Cir. 1997). Adequate written description of genetic material "requires a precise definition, such as by structure, formula, chemical name, or physical properties." *Regents of the University of California v. Eli Lilly & Co.,* 119 F.3d 1559, 1566 (Fed.Cir. 1997), *Fiers v. Revel,* 984 F.2d 1164, 1171 (Fed.Cir. 1993)).

Applicants respectfully submit that the basic *quid pro quo* of the patent system is that the public must receive meaningful disclosure in exchange for being excluded from practicing the invention for a limited period of time. *See, Enzo Biochem, Inc.*, 119 F.3d at 1330. Applicants have met their part of the bargain – they have meaningfully disclosed their nucleic acid molecules by way of stating the specific nucleotide sequence, SEQ ID NO.: 3, which not only provides chemical formula information, but also implicitly provides the structure of the claimed

molecules.[1] In addition, because of the nature of nucleic acid sequences, the disclosed sequence provides properties of the molecules, such as their ability to hybridize with other nucleic acid molecules, to interact with restriction enzymes, etc. Moreover, the disclosure of sequence, structure, and properties are applicable not only to the full-length molecule, but also to fragments of SEQ ID NO.: 3, which Applicants have expressly discussed in the disclosure (see page 12, lines 16-22 for example).

The Examiner's allegation that the claims lack written description support because they "are drawn to fragments and sequences comprising fragments of or the sequences of comprising SEQ ID NO.: 3" does not comport with the requirements of 112 first paragraph written description. Compliance with 112 first paragraph is met for genetic materials when a precise definition, such as by structure, formula, chemical name, or physical properties is set forth by applicant for a patent. Because the disclosure sets forth the sequence of SEQ ID NO.: 3 and fragments thereof,[2] and hence implicitly discloses the structure and formula of these nucleotides, Applicants submit that the disclosure complies with the written description requirement of 112 first paragraph. Moreover, that the disclosed fragments are claimed in the context does not lead to a proper rejection based upon the understood use of comprising terminology in patent claims as discussed immediately below.

Applicants respectfully submit the Examiner's allegation that the disclosure does not meet the written description requirement because it fails to "teach sequences comprising SEQ ID NO.: 3 for instance containing the gene coding region for the TIGR gene" is inconsistent with the

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[1] Applicants submit that the disclosure of a nucleotide sequence implicitly discloses the molecules' structure as an artisan could write down the chemical structure, including the atoms and bonds involved, based upon the disclosed nucleotide sequence.

[2] See page 28, lines 1-8 for example.

understood use of "comprising" terminology in patent claims. The aforementioned disclosure of formula and structure, by virtue of disclosure of nucleotide sequence, is not altered by the incorporation of the claimed sequences into other nucleotide constructs. Thus, the use of open claiming language (comprising) does not alter the fact that a skilled artisan would readily envision adequate written description support for the claimed nucleic acids in the context of a larger construct. It is well-established that use of the transitional term "comprising" leaves the claims "open for the inclusion of unspecified ingredients even in major amounts." *Ex parte Davis*, 80 U.S.P.Q. 448, 450 (BPAI 1948). The fact that nucleic acid sequences may be added to either or both ends of the recited sequence, such as when incorporated into a circular vector, does not properly lead to a conclusion that there is insufficient written description support.

With regard to the Examiner's allegation that the specification fails to teach "specific regions by way of sequence structure which correlate to the functional regions for initiation of TIGR gene expression." Applicants respectfully submit that as set forth above, they have met their burden under 112 first paragraph by disclosing SEQ ID NO.: 3, and thereby the formula and structure of the claimed nucleic acids. Applicants respectfully submit that the Examiner, by asserting a requirement to teach specific sequences and structures that correlate with TIGR gene expression, is imposing additional requirements on patentability in excess of those necessary to meet the written description requirement. Applicants maintain that they need not identify and correlate functional regions of the claimed nucleic acids to meet the written description requirement where they have provided "a precise definition, such as by structure [and] formula." *See, Regents of the University of California,* 119 F.3d at 1566, *supra.*[3]

[3] Applicants respectfully submit that although not necessary to meet the requirement for written description, the disclosure is replete with a discussion of the transcription factor binding sites that

In the matter of the Examiner's reliance on MPEP 2163 for the proposition that "invention as a whole, any nucleic acid fragment of SEQ ID NO.: 3 or any larger sequence comprising SEQ ID NO.: 3, is not adequately described in view of the lack of identifying characteristics," Applicants respectfully submit the Examiner's assertion is inconsistent with MPEP 2163. Applicants note that not only is the Examiner's position in conflict with the material actually included in the quote from MPEP 2163, but the quoted material contains ellipses that stand in place of pages of omitted text, including passages that are relevant to the issue.

The opening passages quoted from MPEP 2163 by the Examiner at page 4 of the September 10, 2002 Office Action:

> The claimed invention as whole may not be adequately described where an invention is described solely in terms of a method of its making coupled with its function and there is no described or art-recognized correlation or relationship between the structure of the invention and its function. A biomolecule sequence described only by a functional characteristic, without disclosed correlation between that function and the structure of the sequence, normally is not a sufficient identifying characteristic for written description purposes, even when accompanied by a method of obtaining a claimed sequence

(quoted from MPEP 2163 I. A) is directed to claims where the molecules are described by function and methods of obtaining a molecule. This contrasts with, and is inapplicable to, the instant situation, where Applicants have *disclosed the actual sequence*, and implicitly the formula and structure, of the claimed biomolecules. Applicants further submit that the Examiner has ignored the further discussion in MPEP 2163 II. A.3 (a), stating that identifying characteristics of a biomolecule may include a sequence or a structure and the discussion of

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map to the promoter region. For example, the specification starting at page 25 line 29 and extending through at least page 27 discusses upstream motifs by their sequence locations, and the location of transcription start sites is also given (see figure 1E).

Lockwood v. American Airlines holding the written description requirement may be satisfied by using such descriptive means as ... structures ... formulas ... that fully set forth the invention. 107 F.3d at 1572. As discussed above, Applicants have provided both the structure and formula of the nucleic acids and have thus met the written description requirement.

The following passage, that the Examiner quoted from the MPEP "A lack of written description issue also arises if the knowledge and level of skill in the art would not permit one skilled in the art to immediately envisage the product claimed from the disclosed process..." (quoted from MPEP 2163 I. A), is also inapplicable to the instant situation as Applicants have not presented product by process claims. Moreover, a skilled artisan would be able to envisage the products based upon the sequence information Applicants have disclosed.

The last passage of the MPEP paragraph by the Examiner,

> The written description requirement for a claimed genus may be satisfied through a sufficient description of a representative number of species by actual reduction to practice..., reduction to drawings..., or by disclosure relevant, identifying characteristics, i.e., structure or other physical and or chemical properties, by functional characteristics coupled with a known disclosed correlation between function and structure, or by combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus.

(partially quoted from MPEP 2163 II. A.3 (a) (ii)), is directed to written description for genus claims wherein fewer than all of the members of a genus have been disclosed. Applicants respectfully submit that this is not relevant to the instant analysis as Applicants have disclosed SEQ ID NO.: 3 and implicitly all of the fragments that can be derived therefrom. Applicants maintain that they have provided sufficient identifying characteristics and that they have provided "a precise definition, such as by structure [and] formula" for every nucleic acid claimed, and thereby have met the burden set forth in *Fiers v. Revel* 984 F.2d 1164 (Fed. Cir. 1993), *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 U.S.P.Q.2d 1016 (Fed. Cir. 1991), *Fiddles v. Baird*,

30 U.S.P.Q.2d 1481, 1483 (Fed. Cir. 1993) and *Regents of the University of California v. Eli Lilly & Co.* 119 F.3d 1159 (Fed. Cir. 1997).[4]

Claims 80, 103, 106, 108, 109, 112, and 114 also stand rejected under 35 U.S.C. §112, first paragraph, as allegedly lacking written description based upon the assertion that the cells of these claims "are not adequately described" for any cell, but only an isolated cell in view of the unpredictability in the art for making recombinant cells *in vivo*. Applicants respectfully disagree and note that the Examiner is relying on two pieces of art directed to *in vivo* gene therapy. Applicants respectfully note that genetic material may be introduced into cells in a variety of ways, any number of which are disclosed by Applicants in the specification. In addition, other techniques may be used to introduce genetic material into cells, including forming transgenic organisms bearing the introduced genetic material in every cell.[5] Because there exists a diversity of means by which a cell may be engineered to contain a specific nucleotide construct, the Examiner's reliance on two articles on the topic of gene therapy fails to establish that the disclosure fails to adequately describe a cell bearing the claimed nucleotides *in vivo*.

In view of the foregoing, Applicants contend that they have met the requirements of 35 U.S.C. § 112 first paragraph and respectfully request the withdrawal of the rejections of record. Applicants submit that the claims are in condition for allowance and solicit a notice of allowability at the earliest possible time.

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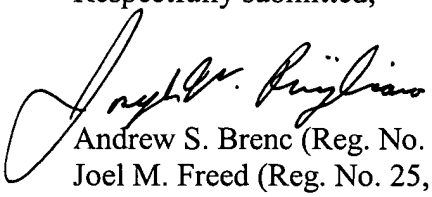
[4] Applicants respectfully submit that although not necessary to meet the requirement for written description, the disclosure is replete with a discussion of the transcription factor binding sites that map to the promoter region. For example, the specification starting at page 25 line 29 and extending through at least page 27 discusses upstream motifs by their sequence locations, and the location of transcription start sites is also given (see figure 1E).

[5] It is well-established patent jurisprudence that Applicants need not teach "conventional and well-known genetic engineering techniques." *See e.g., Ajinomoto Co. v. Archer-Daniels-Midland Co.*, 228 F.3d 1338, 1345, 56 U.S.P.Q.2d 1332, 1337 (Fed. Cir. 2000).

Should the Examiner have any questions regarding this application, the Examiner is encouraged to contact Applicant's undersigned representative at 202-942-5174.

The U.S. Patent and Trademark Office is hereby authorized to charge any fee deficiency, or credit any overpayment, to our Deposit Account No. 50-2387.

Respectfully submitted,



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Date: December 9, 2002

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